

# NIAAA SPECTRUM

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Institute on Alcohol Abuse and Alcoholism

## FEATURE

### ALCOHOL AND “DEATHS OF DESPAIR”



In 2015, Princeton University economists Anne Case, Ph.D., and Angus Deaton, Ph.D., reported something unexpected. After decreasing since the end of World War II, rates of death began to increase in the United States for people in some groups. The rise in deaths was driven primarily by drug and alcohol overdoses, suicides, and liver disease. These conditions, in turn, were related to declining quality of life—reduced physical and mental health, increases in chronic pain, financial difficulties, and serious mental illness. Given the nature of these deaths, Drs. Case and Deaton referred to them as “deaths of despair.” They reported that the increase in mortality occurred primarily among 45–54-year-old non-Hispanic, White men and women.

A subsequent study led by researchers at Virginia Commonwealth University found an increase in deaths of despair among people ages 25–64 in a variety of groups, including non-Hispanic Whites, non-Hispanic American Indians and Alaskan Natives, non-Hispanic Blacks, Hispanics, and non-Hispanic Asians and Pacific Islanders. Although drug overdoses, alcohol-associated liver disease (AALD), and suicides played major roles in these increases, deaths also increased for falls and other injuries, heart disease, respiratory conditions, cancers, and other causes. And it appears that the United States is not alone, as deaths of despair are on the rise among middle-aged men and women in England, too.

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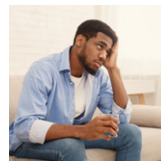
- 1 Alcohol and “Deaths of Despair”

### NEWS FROM THE FIELD



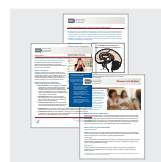
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## NEWS FROM THE FIELD

## STEPPED ALCOHOL TREATMENT IMPROVES HIV AND ALCOHOL OUTCOMES



Increasing the intensity of treatment for alcohol use disorder (AUD) over the time course of treatment reduces alcohol consumption among people living with human immunodeficiency virus (HIV) and AUD, according to new

clinical research supported by NIAAA. In the study, led by researchers at Yale University, this stepped approach to AUD treatment also reduced viral load (amount of HIV present in the blood) and improved other HIV-related disease

measures in this patient population. A report of the study appears in *The Lancet HIV*.

“These research findings demonstrate the potential of integrated treatment for AUD and HIV to improve health outcomes and provide support for integrating AUD treatment in HIV and other healthcare settings,” says NIAAA Director George F. Koob, Ph.D.

Alcohol misuse can increase risky behaviors that increase the likelihood of acquiring HIV, speed the progression of the disease, and make it harder to follow medication regimens. Previous studies have linked drinking, even at low levels, to greater risk of death for people with HIV.

In the present study, E. Jennifer Edelman, M.D., M.H.S., and her colleagues at Yale studied 5 U.S. Department of Veterans Affairs–based HIV clinics with 128 people who were HIV-positive and had AUD. They

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## SPOTLIGHT

## THE COMPLEX RELATIONSHIP BETWEEN ALCOHOL AND PAIN



The relationship between alcohol and pain is a complicated one. It is a common belief that alcohol dulls pain, yet research shows that sometimes alcohol can make pain worse.

Understanding the complex relationship between alcohol and pain is an important area of research for NIAAA. In 2016, about 20 percent of adults (50 million people) in the United States had chronic pain, defined as pain most days in the previous 6 months. Recent studies suggest that around 1 in 4 adults in chronic pain reports self-medicating with alcohol, and 43–73 percent of people with alcohol use disorder (AUD) report experiencing chronic pain. An improved understanding of

the effects of alcohol on pain, the role of pain in alcohol misuse, and potential interactions between alcohol and opioids during pain treatment hopefully will improve treatment outcomes for patients in pain.

Alcohol has been found to alleviate physical pain, but it requires doses consistent with binge drinking to do so. Binge drinking is defined as drinking enough to bring blood alcohol concentration (BAC) levels to 0.08 percent, which typically occurs after 4 drinks for women and 5 drinks for men in about 2 hours. A recent analysis of the findings from 18 studies on alcohol and pain concluded that

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## FEATURE: Alcohol and “Deaths of Despair” . . . Continued from page 1

Alcohol plays a prominent role in deaths of despair, contributing to overdoses, suicides, and liver disease, as well as to a broad range of other disease states that lead to mortality. Alcohol use is increasing among middle-aged adults in the United States and is more common when people are faced with stressful circumstances, such as job loss, divorce, economic downturns, chronic pain, or psychiatric conditions—all factors related to deaths of despair.

“I consider alcohol the elephant in the room when it comes to the mortality trends revealed in these recent studies,” says NIAAA Director George F. Koob, Ph.D. “People are more likely to drink excessively to help cope with significant challenges of life, but this is a slippery slope that commonly leads to more pain and misery.”

A significant contributor to deaths of despair, drug overdose deaths in the United States increased from 16,849


in 1999 to 70,237 in 2017. The largest increase involved opioids, which claimed nearly 400,000 lives during that period. Alcohol plays a role in about 1 in 5 overdose deaths involving opioids. Alcohol and opioid misuse share common underlying risk factors related to deaths of despair, including mood disorders, suicidal ideation, a history of trauma, and chronic pain. (For more information, see the Spotlight story “The Complex Relationship Between Alcohol and Pain.”) A recent study revealed just how dangerous the combination of opioids and alcohol can be. Both alcohol and opioids can cause death by suppressing areas near the base of the brain that control breathing. When researchers gave healthy younger and older adults 20 mg of oxycodone, breathing was reduced by 28 percent. When they combined this dose of oxycodone with enough alcohol to raise subjects’ blood alcohol concentration (BAC) to 0.1 percent—comparable

to having about 4 drinks for women or 5 for men in an hour—breathing decreased by another 19 percent. The impact was bigger in older drinkers. Alcohol contributes to other drug overdoses as well. Deaths due to overdoses on benzodiazepines, medications often used to treat anxiety, have increased in recent years, and alcohol contributes to roughly 1 in 5 such deaths.

Drs. Case and Deaton reported that deaths from liver disease are key contributors to the increase in deaths of despair. The liver—the largest organ in the body—helps digest food, store energy, and detoxify alcohol and other harmful substances. The number of deaths in the United States each year from diseases of the liver is rising and reached 41,743 in 2017. Roughly half of these deaths were caused by AALD, particularly cirrhosis. Deaths due to

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## NOTEWORTHY



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### Interrupted Memories: Alcohol-Induced Blackouts

Drinking to the point of a blackout has gained pop culture notoriety in recent years. Blackouts are typically associated with consuming excessive amounts of alcohol that can lead to impaired memory of events that transpired while intoxicated, and a drastically increased risk of injuries and other harms. They can occur in anyone who drinks alcohol, no matter their age or level of experience with drinking. In this fact sheet, we will take a sober look at this common but deeply concerning consequence of alcohol misuse.



National Institute on Alcohol Abuse and Alcoholism


### Hangovers

For many people, a night of drinking can lead to a painful morning after and the dreaded effects of a hangover. What does science tell us about this phenomenon? What causes the typical symptoms of a hangover? And the question perhaps as old as hangovers themselves—are there any real remedies?

**What is a Hangover?**  
A hangover refers to a set of symptoms that occur as a consequence of excessive alcohol use. Typical symptoms include fatigue, weakness, thirst, headache, muscle aches, nausea, stomach pain, vertigo, sensitivity to light and sound, anxiety, irritability, sweating, and increased blood pressure. A hangover can vary from person to person.

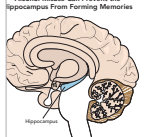
**What Causes Hangover Symptoms?**  
A number of factors can contribute to hangovers:

- Mild dehydration:** Alcohol suppresses the release of vasopressin, a hormone produced by the brain that sends signals to the kidneys causing them to retain water. As a result, alcohol increases urination and causes loss of fluids. The mild dehydration that results likely contributes to hangover symptoms such as thirst, fatigue, and a headache.
- Disrupted sleep:** People may fall asleep faster after drinking alcohol, but their sleep is fragmented, and they tend to wake up earlier. This contributes to fatigue, as well as loss of productivity.
- Gastrointestinal irritation:** Alcohol directly irritates the lining of the stomach and increases acid release. This can lead to nausea and stomach discomfort.
- Inflammation:** Alcohol increases inflammation in the body, inflammation of the liver people feel when they are sick, so it may play a role in hangover symptoms.
- Acetaldehyde exposure:** Alcohol metabolism, primarily by the liver, creates acetaldehyde, a toxic, even more potent, which contributes to inflammation, pain, gastrointestinal tract, and other organs.




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### Alcohol Misuse Can Prevent the Hippocampus From Forming Memories



Alcohol misuse can prevent the hippocampus from forming memories. The hippocampus is a part of the brain that is responsible for learning and memory. When alcohol is consumed, it can interfere with the hippocampus's ability to form new memories, leading to blackouts.



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### Women and Alcohol

Research shows that alcohol use and misuse among women are increasing. While alcohol misuse by anyone presents serious public health concerns, women who drink have a higher risk of certain alcohol-related problems compared to men. It is important that women be aware of these health risks and of the U.S. dietary guidelines, which recommend no more than 1 drink per day for women, so they make informed decisions about alcohol use.

**Why Do Women Face Higher Risks?**  
Studies show that women start to have alcohol-related problems sooner and at lower drinking levels than men and for multiple reasons. On average, women weigh less than men. Also, alcohol resides predominantly in body water, and, pound for pound, women have less water in their bodies than men. This means that after a woman and a man of the same weight drink the same amount of alcohol, the woman's blood alcohol concentration (BAC, the amount of alcohol in the blood) will tend to be higher, putting her at greater risk for harm. Other biological differences may contribute as well.

**What Are the Long-Term Health Risks?**  
**Alcohol Use Disorder**  
Alcohol use disorder (AUD) is a chronic relapsing brain disorder characterized by an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences. AUD can range from mild to severe, and recovery is possible regardless of severity.

**Liver Damage**  
Women who regularly misuse alcohol are more likely than men who drink the same amount to develop alcoholic liver disease, a potentially fatal alcohol-related liver condition. This pattern of drinking can also lead to cirrhosis (permanent liver scarring).

**Heart Disease**  
Long-term alcohol misuse is a leading cause of heart disease. Women are more susceptible to alcohol-related heart disease than men, even though they may consume less alcohol over their lifetime than men.

## NEW AND UPDATED NIAAA PUBLICATIONS

NIAAA recently released new publications on topics of increased interest from the media and general public, as well as from visitors to the NIAAA exhibit booth at professional meetings.

These additions to NIAAA's factsheet collection are Hangovers and Interrupted Memories: Alcohol-Induced Blackouts.

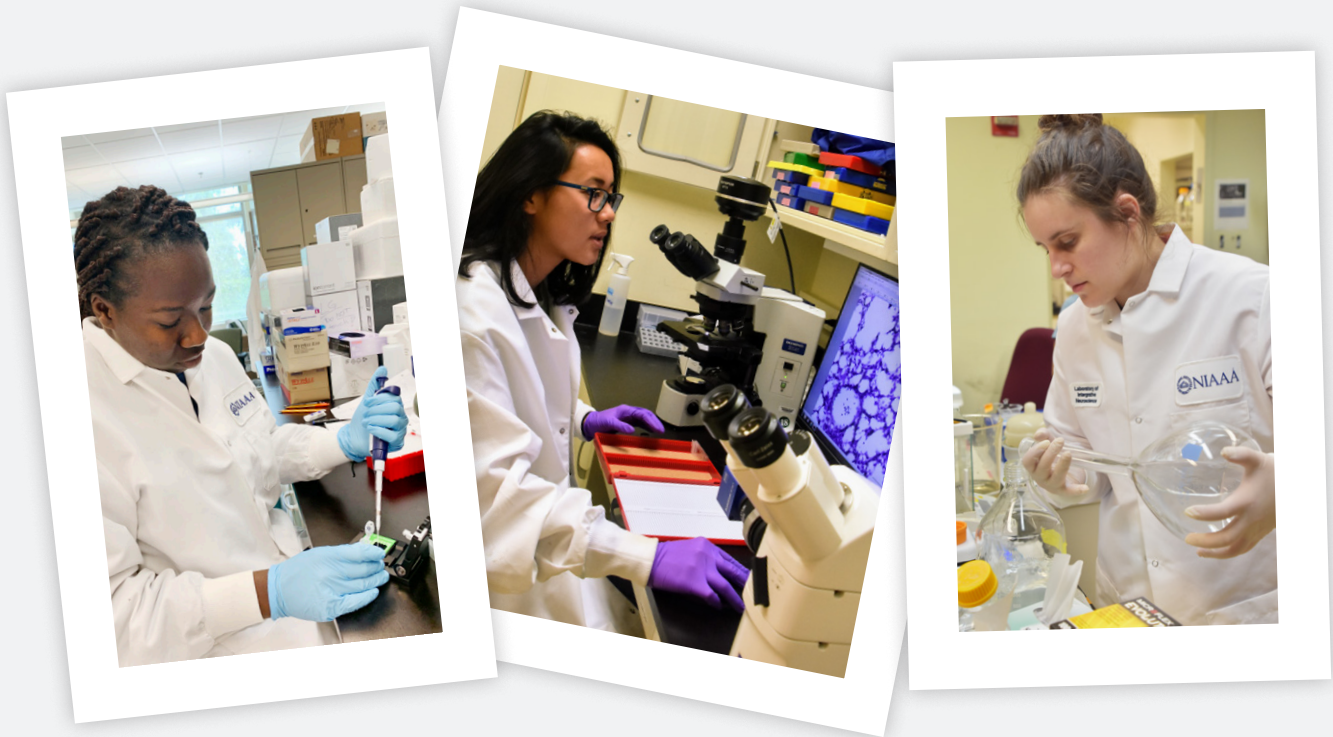
In addition, the NIAAA factsheet on Women and Alcohol was revised recently to reflect new statistics and updated research information.

You can view and download these and other NIAAA public education materials at <https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets>.



## NIAAA@WORK

## TRAINING TOMORROW'S ALCOHOL RESEARCHERS



Pictured, left to right: Caroline Djakuduel, Laboratory of Neurogenetics; Mei Mei Zuo, Laboratory of Physiologic Studies; and Riley Paulsen, Laboratory for Integrative Neuroscience

Each summer, NIAAA's Division of Intramural Clinical and Biological Research (DICBR) hosts high school, college, and graduate students from across the nation. These student-trainees work in the DICBR laboratories, gain research skills, and receive mentoring from NIAAA researchers.

This year, some of the student projects investigated alcohol-induced lung injury, alcohol's role in inflammation, the neurobiology of stress and addiction, health disparities in substance use disorders, the impact of cannabis on sleep, and brain signaling during reward-seeking behaviors. Student-trainees presented their research at the National Institutes of Health Poster Day in August.

## FEATURE: Alcohol and “Deaths of Despair” . . . Continued from page 3

AALD are more common in adults over the age of 45 than in younger drinkers, but the biggest increases in such deaths in recent years occurred among young adults ages 25–34.

Rates of suicide in the United States are increasing and are higher now than at any time since World War II. More than 47,000 people died from suicide in 2017, and suicide is the fourth-leading cause of death for people ages 35–54.

Alcohol misuse both follows and contributes to mental health conditions that increase the risk of suicide. People with alcohol use disorder (AUD) are twice as likely as those without AUD to experience major depression, five times as likely to suffer from bipolar disorder, and three times as likely to experience post-traumatic stress disorder. People with AUD are much more likely to contemplate suicide, and alcohol often plays a role in suicide attempts. Estimates suggest that nearly 1 in 4 males and 1 in 5 females are intoxicated—with BAC levels of 0.08 percent or more—at the time of a suicide.

In addition to overdoses, liver disease, and suicides, alcohol contributes to

mortality in other ways that might add to deaths of despair. Alcohol plays a role in roughly 3.5 percent of all cancer deaths in the United States. For women, the risk of breast cancer increases with less than 1 drink per day. Compared to women who consumed fewer than 60 drinks in a typical year, those consuming 60–229 drinks (about 0.6 drinks per day, on average) were 20 percent more likely to develop breast cancer. Research also has shown that people who drink excessively have a greater risk of cancers of the mouth, esophagus, larynx, pharynx, liver, colon, and rectum.

Alcohol also is a common factor in deaths from injuries. The U.S. Centers for Disease Control and Prevention (2013) estimates that alcohol contributes to 32 percent of deaths from falls, 42 percent of deaths from fires, 47 percent of deaths from homicides, and 34 percent of deaths from drownings.

Alcohol is not the only factor driving the increase in deaths of despair, but raising awareness of the health risks posed by alcohol and the dangers of

using alcohol to cope with challenges in life could help reduce the number of such deaths.

According to Dr. Koob, “Perhaps our most fundamental responsibility is to ensure that all people possess basic knowledge of alcohol’s immediate and long-term health effects, and that all healthcare professionals, from trainees through senior clinicians, make alcohol assessment an integral part of every interaction with patients.” Currently, 85 percent of adults ages 18 and older in the United States see a doctor or other healthcare professional each year, but fewer than 1 in 4 report being asked during a visit in the past year how often or how much they drink.

To learn more about the health risks posed by alcohol and to evaluate whether your relationship with alcohol might constitute AUD, please visit the NIAAA website, *Rethinking Drinking*, at <https://www.rethinkingdrinking.niaaa.nih.gov>. To explore treatment options and to locate a treatment provider, please visit the NIAAA Alcohol Treatment Navigator, at <https://alcoholtreatment.niaaa.nih.gov>.

### References:

- Centers for Disease Control and Prevention. Alcohol and Public Health: Alcohol-Related Disease Impact (ARDI). Average for United States 2006–2010 Alcohol-Attributable Deaths Due to Excessive Alcohol Use. <https://go.usa.gov/xym4p>. Accessed July 15, 2019.
- Case, A.; and Deaton, A. Rising morbidity and mortality in midlife among White non-Hispanic Americans in the 21st century. *Proceedings of the National Academy of Science of the United States of America* 112(49):15078–15083, 2015. PMID: 26575631
- Woolf, S.H.; Chapman, D.A.; Buchanich, J.M.; Bobby, K.J.; Zimmerman, E.B.; and Blackburn, S.M. Changes in midlife death rates across racial and ethnic groups in the United States: Systematic analysis of vital statistics. *BMJ* 362:k3096, 2018. PMID: 30111554
- O’Keefe, E.L.; DiNicolantonio, J.J.; O’Keefe, J.H.; and Lavie, C.J. Alcohol and CV health: Jekyll and Hyde J-curves. *Progress in Cardiovascular Diseases* 61(1):68–75, 2018. PMID: 29458056
- Barr, T.; Helms, C.; Grant, K.; and Messaoudi, I. Opposing effects of alcohol on the immune system. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 65:242–251, 2016. PMID: 26375241
- Nelson, D.E.; Jarman, D.W.; Rehm, J.; Greenfield, T.K.; Rey, G.; Kerr, W.C.; Miller, P.; Shield, K.D.; Ye, Y.; and Naimi, T.S. Alcohol-attributable cancer deaths and years of potential life lost in the United States. *American Journal of Public Health* 103(4):641–648, 2013. PMID: 23409916
- Shield, K.D.; Soerjomataram, I.; and Rehm, J. Alcohol use and breast cancer: A critical review. *Alcoholism: Clinical and Experimental Research* 40(6):1166–1181, 2016. PMID: 27130687
- Fedirko, V.; Tramacere, I.; Bagnardi, V.; Rota, M.; Scotti, L.; Islami, F.; Negri, E.; Straif, K.; Romieu, I.; La Vecchia, C.; Boffetta, P.; and Jenab, M. Alcohol drinking and colorectal cancer risk: An overall and dose-response meta-analysis of published studies. *Annals of Oncology* 22(9):1958–1972, 2011. PMID: 21307158
- Tapper, E.B.; and Parikh, N.D. Mortality due to cirrhosis and liver cancer in the United States, 1999–2016: Observational study. *BMJ* 362:k2817, 2018. PMID: 30021785

## NEWS FROM THE FIELD: *Stepped Alcohol Treatment . . . Continued from page 2*

investigated integrated stepped alcohol treatment (ISAT)—an approach that involves consecutive steps of increasing the intensity of AUD treatment if lower-intensity treatment does not produce desired results.

Although no differences in drinks per week consumed or HIV outcomes were found between the ISAT group and control group at 6 months, at the 12-month followup, individuals receiving ISAT were found to have fared better—reporting fewer drinks

consumed per drinking day and a greater percentage of days abstinent.

“Importantly, we also observed that participants randomized to stepped AUD treatment were more likely to achieve an undetectable HIV viral load,”

says Dr. Edelman. “We believe that with decreased alcohol consumption, participants in the ISAT group were more likely to take their HIV medications consistently, translating into improved HIV viral control.”

### Reference:

Edelman, E.J.; Maisto, S.A.; Hansen, N.B.; Cutter, C.J.; Dziura, J.; Deng, Y.; Fiellin, L.E.; O'Connor, P.G.; Bedimo, R.; Gibert, C.L.; Marconi, V.C.; Rimland, D.; Rodriguez-Barradas, M.C.; Simberkoff, M.S.; Tate, J.P.; Justice, A.C.; Bryant, K.J.; and Fiellin, D.A. Integrated stepped alcohol treatment for patients with HIV and alcohol use disorder: A randomised controlled trial. *The Lancet HIV* 6(8):e509–e517, 2019. PMID: 31109915

## SPOTLIGHT: *The Complex Relationship . . . Continued from page 2*

a BAC of 0.08 percent produces a small increase in pain threshold and a reduction in pain intensity. These findings could help explain why some people with chronic pain drink excessively. Unfortunately, reaching BAC levels this high also is associated with unintentional injuries, violence, traffic fatalities, and other consequences. And long-term excessive drinking makes physical pain worse. In a group of 30 men in treatment for AUD, sensitivity to pain increased early in abstinence.

People also sometimes use alcohol in an effort to cope with emotional pain. Unfortunately, as with physical pain, the temporary reprieve alcohol might offer gives way to an increase in emotional pain when the alcohol wears off. Chronic alcohol misuse can lead to the emergence of a negative emotional state, known as hyperkatifeia, in between episodes of drinking. The resulting irritability, dysphoria, and anxiety fuel further alcohol use. As with physical pain, drinking alcohol to cope with emotional pain makes the situation worse. (For more information, see the Feature story “Alcohol and ‘Deaths of Despair.’”)

Opioid analgesics commonly are prescribed to treat physical pain and often are misused to cope with emotional pain. Used separately, alcohol and opioids can cause overdose deaths by suppressing areas in the brain stem

that control breathing. Using alcohol and opioids together amplifies the danger. Research suggests that alcohol plays a role in around 1 in 5 deaths from opioid overdoses.

Because the mechanisms by which alcohol and opioids reduce physical and emotional pain overlap, regular use of one drug diminishes the effects of the other. For instance, when researchers examined opioid pain medication use after abdominal surgery in more than 4,000 patients, they found that frequent alcohol consumption was associated with increased opioid use for pain control. Similarly, in rats allowed to drink alcohol for 8 weeks, opioids became less effective at reducing physical pain. Withdrawal from opioids, like withdrawal from alcohol, leads to the emotional misery of hyperkatifeia.

As part of the National Institutes of Health Helping to End Addiction Long-Term (HEAL) initiative, NIAAA is encouraging studies to develop and validate biomarkers of comorbid alcohol misuse and chronic pain and that address alcohol misuse in the context of chronic pain management. NIAAA also encourages research on the impact of alcohol and sleep disturbances on pain through a new funding opportunity (PA-19-200). These efforts, among others, should shed light on how alcohol affects pain and vice versa and could have implications for both treating AUD and managing chronic pain.

### References:

- Koob, G.F. Neurobiology of opioid addiction: Opponent process, hyperkatifeia, and negative reinforcement. *Biological Psychiatry* June 12, 2019. PMID: 31400808
- Rogers, A.H.; Kauffman, B.Y.; Bakhshaie, J.; McHugh, R.K.; Ditte, J.W.; and Zvolensky, M.J. Anxiety sensitivity and opioid misuse among opioid-using adults with chronic pain. *The American Journal of Drug and Alcohol Abuse* 45(5):470–478, 2019. PMID: 30896985
- Thompson, T.; Oram, C.; Correll, C.U.; Tsermentseli, S.; and Stubbs, B. Analgesic effects of alcohol: A systematic review and meta-analysis of controlled experimental studies in healthy participants. *The Journal of Pain* 18(5):499–510, 2017. PMID: 27919773
- Witkiewitz, K.; and Vowles, K.E. Alcohol and opioid use, co-use, and chronic pain in the context of the opioid epidemic: A critical review. *Alcoholism: Clinical and Experimental Research* 42(3):478–488, 2018. PMID: 29314075
- Zale, E.L.; Maisto, S.A.; and Ditte, J.W. Interrelations between pain and alcohol: An integrative review. *Clinical Psychology Review* 37:57–71, 2015. PMID: 25766100
- Edwards, S.; Vendruscolo, L.F.; Schlosburg, J.E.; Misra, K.K.; Wee, S.; Park, P.E.; Schulteis, G.; and Koob, G.F. Development of mechanical hypersensitivity in rats during heroin and ethanol dependence: Alleviation by CRF<sub>1</sub> receptor antagonism. *Neuropharmacology* 62(2):1142–1151, 2012. PMID: 22119954



## 5 QUESTIONS WITH . . .

### MARK EGLI, PH.D.

*Deputy Director of the Division of Neuroscience and Behavior*



#### 1 As the Deputy Director of the Division of Neuroscience and Behavior (DNB), how would you characterize DNB's research program?

DNB's portfolio comprises a broad range of neuroscience research from genes to behavior. This research covers alcohol exposure across the lifespan, including developmental transitions from adolescence to adulthood and into aging. In addition, alcohol use disorder [AUD] is a complex disorder, and our research program over time has expanded to include studies on emotional states, sleep disturbances, social competence, cognitive function, and pain.

#### 2 What are some emerging research areas DNB has been exploring?

Susceptibility and resilience to AUD have been explained by genes—DNA variants—and environment; however, we're discovering that there is a third mechanism, epigenetics, that bridges these two areas. Investigators recently showed that alcohol exposure may cause non-protein-coding RNAs

(microRNA, long noncoding RNA, etc.) to reprogram protein-coding genes to influence their expression in specific brain regions of both early-stage and late-onset AUD patients. Some of the genes are related to stress and occur in brain regions, such as the amygdala, that are implicated in AUD. This research finding confirms data from animal models and suggests an important mechanism underlying the development of AUD. There's a possibility that alcohol-induced epigenetic changes are transmitted to offspring, putting future generations at risk for AUD.

We are also exploring ways to promote research involving social isolation, which puts people at risk for many negative health conditions, including AUD. It's important to understand the neurobiological impact of loneliness and loss of social attachment as they relate to risk for AUD and to recovery. Harmful effects of drinking on social attachment and social effectiveness also need to be better understood, as this may contribute to depression and suicide.

Binge drinking is increasing in aging populations. We've collaborated with the National Institute on Aging to fund administrative supplements on research examining the effects of alcohol on Alzheimer's disease and related dementias.

#### 3 Pain research is an area in which you've expanded support—how did that evolve?

DNB has a strong pain research program thanks to Dr. Soundar Regunathan's efforts as NIAAA's Program Director. In 2010, we developed several symposia and new funding opportunity announcements. Around the same time, NIAAA Director Dr. George F. Koob, Dr. Scott Edwards, and I wrote a review on this topic. A growing body of research has shown that brain systems supporting pain perception, particularly emotional pain,

overlap with those involved in alcohol and opioid use disorders. In rodent models and in humans, alcohol causes pain. It implies that chronic alcohol use increases pain, and that pain provokes drinking because of the effects on shared neural circuitry.

More recently, it's become clear that alcohol is a major factor in the increased "deaths of despair" in the United States, including not only being responsible for alcohol-associated liver disease, but also contributing to opioid overdoses and suicides. For some, AUD along with chronic pain and opioid use disorder may be facets of a mechanistically integrated syndrome with accidental overdose and suicide as outcomes. We have identified several "sinkholes," whereby alcohol consumption and phenomena such as pain, opioid use, impulsivity, and negative affect enter into positive-feedback relationships, meaning changes in one of these domains (e.g., elevated alcohol misuse) can amplify one or more of the others (e.g., increased opioid misuse). This can lead to deadly consequences. We hope to stimulate research to provide a better mechanistic understanding of those relationships.

#### 4 Looking ahead, where do you see the DNB program heading?

Big and bold. My sense is that there are major paradigm shifts ahead. Increased computational capabilities will allow us to analyze large datasets from diverse sources such as the National Institutes of Health [NIH]-funded Adolescent Brain Cognitive Development [ABCD] study and the NIH All of Us initiative. The National Institute of Mental Health is leading efforts in the emerging field of computational psychiatry, with the aim of integrating observations across biological and behavioral systems over time through large-scale modeling.

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The goal is to identify conditions that lead to disease and to suggest effective therapies. Much of this work will be applicable to AUD.

In addition, the NIH Brain Research Through Advancing Innovative Neurotechnologies [BRAIN] initiative is a major investment in technologies to advance spatial and temporal resolution of brain function measures. There will also be methods to measure behavior from previously inaccessible sources and with greater temporal resolution. Also very exciting is that

the experimental and computational tools generated in the past 5 years by the BRAIN initiative are becoming available to our alcohol researchers.

NIAAA also encourages studies through the Small Business Innovation Research [SBIR] program that apply data science methods to expand analytical capabilities in alcohol research. I think the new technologies and paradigms will provide opportunities for researchers to perform studies that better explain the great diversity of AUD among affected individuals.

**5** Outside of work, people say you're a great harmonica player! How did that get started?

I also play clarinet, and my ability to apply woodwind techniques to the harmonica makes people think I'm a more accomplished harmonica player than I really am. My cat likes the sound of blues music for some reason and will sit on my lap and meow along when I play. I played in a blues band in high school, but these days it's just me and Sophie the cat.

### ABOUT US

*NIAAA Spectrum* is NIAAA's triannual webzine. With engaging feature articles, short news updates, and colorful graphics, *NIAAA Spectrum* offers accessible and relevant information on NIAAA and the alcohol research field.

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**National Institute on Alcohol Abuse and Alcoholism (NIAAA)**

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